

KANDA et al
Serial No. 09/971,773

Q¹ bound to 6-position of *N*-acetylglucosamine in the reducing end through $\alpha(1\rightarrow6)$ glycosyl bond in the complex *N*-glycoside-linked sugar chain is decreased or deleted.

Q² 12. (Amended) The CHO cell according to claim 4, wherein the enzyme relating to the modification of a sugar chain in which fucose is bound to 6-position of the *N*-acetylglucosamine in the reducing end through $\alpha(1\rightarrow6)$ glycosyl bond in the complex *N*-glycoside-linked sugar chain is α -1,6-fucosyltransferase.

15. (Amended) The CHO cell according to claim 4, wherein the enzyme activity is decreased or deleted by a technique selected from the group consisting of the following (a), (b), (c), (d) and (e):

- Q³
- (a) a gene disruption technique targeting a gene encoding the enzyme;
 - (b) a technique for introducing a dominant negative mutant of a gene encoding the enzyme;
 - (c) a technique for introducing mutation into the enzyme;
 - (d) a technique for inhibiting transcription and/or translation of a gene encoding the enzyme;
 - (e) a technique for selecting a cell line resistant to a lectin which recognizes a sugar chain in which fucose is bound to 6-position of *N*-acetylglucosamine in the reducing end through $\alpha(1\rightarrow6)$ glycosyl bond in the complex *N*-glycoside-linked sugar chain.

16. (Amended) The CHO cell according to claim 4, which is resistant to at least a lectin which recognizes a sugar chain in which fucose is bound to 6-position of *N*-acetylglucosamine in the reducing end through $\alpha(1\rightarrow6)$ glycosyl bond in the complex *N*-glycoside-linked sugar chain.

17. (Amended) The CHO cell according to claim 4, which produces an antibody composition having higher antibody-dependent cell-mediated cytotoxic activity than an antibody composition produced by its parent CHO cell.

Q⁴ 19. (Amended) The CHO cell according to claim 18, wherein the sugar chain to which fucose is not bound is a complex *N*-glycoside-linked sugar chain in which fucose is not bound to 6-position of *N*-acetylglucosamine in the reducing end through $\alpha(1\rightarrow6)$ glycosyl bond.

Q⁴ 20. (Amended) A method for producing an antibody composition, which comprises culturing the CHO cell according to claim 1 in a medium to produce and accumulate an antibody composition in the culture; and recovering the antibody composition from the culture.

Q⁵ 23. (Amended) A cell in which the activity of an enzyme relating to the synthesis of an intracellular sugar nucleotide, GDP-fucose and/or the activity of an enzyme relating to the modification of a sugar chain wherein fucose is bound to 6-position of *N*-acetylglucosamine in the reducing end through $\alpha(1\rightarrow6)$ glycosyl bond in the complex *N*-glycoside-linked sugar chain is decreased or deleted by a genetic engineering technique.

Q⁶ 31. (Amended) The cell according to claim 23, wherein the enzyme relating to the modification of a sugar chain in which fucose is bound to 6-position of *N*-acetylglucosamine in the reducing end through $\alpha(1\rightarrow6)$ glycosyl bond in the *N*-glycoside-linked sugar chain is α -1,6-fucosyltransferase.

Q⁷ 34. (Amended) The cell according to claim 23, wherein the genetic engineering technique is a technique selected from the group consisting of the following (a), (b), (c) and (d):

- (a) a gene disruption technique targeting a gene encoding the enzyme;
- (b) a technique for introducing a dominant negative mutant of a gene encoding the enzyme;
- (c) a technique for introducing mutation into the enzyme;
- (d) a technique for inhibiting transcription and/or translation of a gene encoding the enzyme.

35. (Amended) The cell according to claim 23, which is resistant to at least a lectin which recognizes a sugar chain in which fucose is bound to 6-position of *N*-acetylglucosamine in the reducing end through $\alpha(1\rightarrow6)$ glycosyl bond in the *N*-glycoside-linked sugar chain.

36. (Amended) The cell according to claim 23, which is a cell selected from the group consisting of the following (a) to (i):

- (a) a CHO cell derived from a Chinese hamster ovary tissue;
- (b) a rat myeloma cell line, YB2/3HL.P2.G11.16Ag.20 cell;

KANDA et al
Serial No. 09/971,773

- Q⁷
- (c) a mouse myeloma cell line, NSO cell;
 - (d) a mouse myeloma cell line, SP2/0-Ag14 cell;
 - (e) a BHK cell derived from a syrian hamster kidney tissue;
 - (f) an antibody-producing hybridoma cell;
 - (g) a human leukemia cell line Namalwa cell;
 - (h) an embryonic stem cell;
 - (i) a fertilized egg cell.

37. (Amended) The cell according to claim 23 into which a gene encoding an antibody molecule is introduced.

Q⁸

39. (Amended) A method for producing an antibody composition, which comprises culturing the cell according to claim 37 in a medium to produce and accumulate the antibody composition in the culture; and recovering the antibody composition from the culture.

41. (Amended) An antibody composition which is produced using the method according to claim 39.

Q⁹

42. (Amended) A transgenic non-human animal or plant or the progenies thereof, comprising a genome which is modified such that the activity of an enzyme relating to the synthesis of an intracellular sugar nucleotide, GDP-fucose and/or the activity of an enzyme relating to the modification of a sugar chain in which fucose is bound to 6-position of *N*-acetylglucosamine in the reducing end through $\alpha(1\rightarrow6)$ glycosyl bond in the *N*-glycoside-linked sugar chain is decreased.

43. (Amended) The transgenic non-human animal or plant or the progenies thereof according to claim 42, wherein a gene encoding the enzyme relating to the synthesis of an intracellular sugar nucleotide, GDP-fucose or a gene encoding the enzyme relating to the modification of a sugar chain in which fucose is bound to 6-position of *N*-acetylglucosamine in the reducing end through $\alpha(1\rightarrow6)$ glycosyl bond in the *N*-glycoside-linked sugar chain is knocked out.

44. (Amended) The transgenic non-human animal or plant or the progenies thereof according to claim 42, wherein the enzyme relating to the synthesis of an

KANDA et al
Serial No. 09/971,773

intracellular sugar nucleotide, GDP-fucose is an enzyme selected from the group consisting of the following (a), (b) and (c):

- (a) GMD (GDP-mannose 4,6-dehydratase);
(b) Fx (GDP-keto-6-deoxymannose 3,5-epimerase, 4-reductase);
(c) GFPP (GDP-beta-L-fucose pyrophosphorylase).

48. (Amended) The transgenic non-human animal or plant or the progenies thereof according to claim 42, wherein the enzyme relating to the modification of a sugar chain in which fucose is bound to 6-position of *N*-acetylglucosamine in the reducing end through $\alpha(1\rightarrow6)$ glycosyl bond in the *N*-glycoside-linked sugar chain is α -1,6-fucosyltransferase.

50. (Amended) The transgenic non-human animal or plant or the progenies thereof according to claim 42, wherein the transgenic non-human animal is an animal selected from the group consisting of cattle, sheep, goat, pig, horse, mouse, rat, fowl, monkey and rabbit.

51. (Amended) A method for producing an antibody composition, which comprises introducing a gene encoding an antibody molecule into the transgenic non-human animal or plant or the progenies thereof according to claim 42; rearing the animal or plant; isolating tissue or body fluid comprising the introduced antibody composition from the reared animal or plant; and recovering the antibody composition from the isolated tissue or body fluid.

53. (Amended) The method according to claim 51, which produces an antibody composition having higher antibody-dependent cell-mediated cytotoxic activity than an antibody composition obtained from a non-human animal or plant or the progenies thereof whose genome is not modified.

54. (Amended) An antibody composition which is produced using the method according to claim 51.